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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,486	11/17/2005	Stefan Laufer	264821US0PCT	6298

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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
MORRIS, PATRICIA L	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
09/12/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/524,486	LAUFER ET AL.	
	Examiner	Art Unit	
	Patricia L. Morris	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,24,27,34 and 36* is/are rejected.

7)☒ Claim(s) *17-23, 25-33, 35 and 38* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 16-38 are under consideration in this application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 3, 2008 has been entered.

Election/Restrictions

Applicants insert that the Examiner must expand the search and examination. The search will **not be expanded** for the reasons clearly set forth in the previous Office actions. Applicants have already been given a reasonable number of compounds. Applicants are essentially claiming millions of compounds and they expect the examiner to search all the claimed compounds and **for the treatment of any and all unknown diseases associated with a disturbed immune system. The compounds are drawn to patentably distinct inventions as clearly set forth in the record.** There is no evidence of record that the instant compounds are able to treat **all disorders associated with a disturbed immune system. A claim to all cytokine-mediated disorders would be considered a reach through to the continuous development of the field. The claims do not meet the requirements of 35 USC 112.**

It is too burdensome for the examiner to search all of the previously noted searches in their respective, completely divergent, areas for the non-elected subject matter, as well, in the limited time provided to search one invention.

The restriction requirement is deemed sound and proper and will be maintained.

Again, this application has been examined to the extent readable on the elected compound wherein R^{10} represents a tetrahydropyran and nonheterocyclic groups, B represents nonheterocyclic groups and R^1-R^7, A, m and n as set forth in claim 1, exclusively. Claim 25 and those dependent thereon all embrace additional heterocycles. Claims 24 and 34 has been examined to the extent readable on the treatment of rheumatoid arthritis since applicants.

Claim Rejections - 35 USC ∋ 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24, 34, 36 and 37 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Contra to applicants' assertions in the instant response, applicants have failed to present any objective evidence that the **elected compounds treat rheumatoid arthritis.** Applicants assert that the data is set forth on page 29 of the specification. The data is silent as to whether any of the elected compounds, *i.e.,* example 54 treats rheumatoid arthritis. Applicants have been given numerous references showing the state of the art and its unpredictability. The examiner is not requiring in vivo data as incorrectly asserted by applicants. Applicants have failed to show any data for the **elected compounds.**

The nature of the invention

The nature of the invention is drawn to the method of using the instant compounds in the treatment of rheumatoid arthritis in which inhibition of release of a cytokine is required.

State of the Prior Art and the level of skill in the art

It is well recognized in the art that there is only a limited understanding of the activities of several cytokines as they relate to their particular biological functions. Odeh (Clinical Immunology and Immunopathology, 83, pp. 103-116, 1997) on page 103 recite that current treatments of rheumatoid arthritis are inadequate. The art recognizes that specific antirreheumatic drugs do not inhibit all cytokines and the mechanisms of action are unclear. See Bondenson, Gen. Pharmac., 29, pp127-150, 1997).

Predictability/unpredictability of the art.

The high degree of unpredictability is well recognized in cytokine inhibition. Rheumatoid arthritis has always been one of the most difficult autoimmune disease to understand and treat. Campbell et al. (Immunology and Cell Biology, 2003, 81, pages 354-366) on page 362, states that a TNF-driven cytokine hierarchy seems untenable, in view of the fact that some TNF

inhibitors have some but not all clinical benefits in patients. The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seeming high level of skill in the art. The existence of these obstacles established that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any treatment regimen on its face.

The amount of direction or guidance and the presence or absence of working examples

The specification is silent as to whether if any compound treats rheumatoid arthritis.

The breadth of the claims

The breadth of the claims are drawn to the treatment of rheumatoid arthritis.

The quantity of experimentation needed

In view of high degree of unpredictability in the art, the limited working example with no results and the fact that the breadth of the claims is not commensurate with that of any objective enablement and that the nexus between inhibition of cytokine release and rheumatoid arthritis has not been established, the quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the compounds and pharmaceutical compositions.

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b). Applicants are also referred to In re Wands, 858 f.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) which

includes the incorporation of the 8 factors recited in Ex parte Foreman, 230 USPQ 546 (Bd. Of App. and Inter 1986).

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by applicants. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants newly added proviso "if R^3 is NR^7COR^{10}, is $R^{8"}$ ito claim 16 is indefinite and unclear to its meaning. How can R^3 represent two groups at the same time? The proviso does not properly state the alternative in an acceptable format such as "If A is B, then C is D" and is therefore confusing. Applicants have not corrected the proviso as alleged in the instant response.

The claims measure the invention. United Carbon Co. v, Binney & Smith., 55 USPQ 381 at 384, col. 1, end of 1st paragraph, Supreme Court of the United States (1942).

The U.S. Court of Claims held to this standard in Lockheed Aircraft Corp. v. United States, 193 USPQ 449, "Claims measure invention and resolution of invention must be based on what is claimed".

The C.C.P.A. in 1978 held "that invention is the subject matter defined by the claims submitted by the applicant. We have consistently held that no applicant should have limitations of the specification read into a claim where no express statement of the limitation is included in the claim": In re Priest, 199 USPQ 11, at 15.

Terminal Disclaimer

The terminal disclaimer filed on July 3, 2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of Ser. no. 10/524,486 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Allowable Subject Matter

Claim 16 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

Claims 17-23 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 25 is objected to as containing nonelected subject matter. The objection may be overcome by limiting the claim to the subject matter indicated as being examinable, supra. A claim so limited would appear allowable

Claims 26-33, 35 and 38 presented in independent form or made dependent on an allowable claim, would appear allowable, otherwise it is objected to as being dependent on a nonallowed claim.

Conclusion

Claims 24, 34, 36 and 37 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia L. Morris whose telephone number is (571) 272-0688. The examiner can normally be reached on Mondays through Fridays.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Patricia L. Morris/
Primary Examiner, Art Unit 1625

plm
September 8, 2008